## REMARKS

Claims 18, 19, 21 and 24 are pending. Claims 1, 10 and 22 have been cancelled. Claims 18, 19 and 24 have been amended. Support for the newly amended claims can be found throughout the specification. More specifically, support can be found in Example 6 starting on page 50. The Examples describes the administration of zoledronic acid to protect against cancerous bone loss, cortical thinning and reduction of bone loss by daily oral administration of letrozole.

In the Advisory Action dated December 9, 2008, the Examiner withdrew the 35 U.S.C. 112, first paragraph rejection but maintains the 103(a) rejection of claims 1, 10, 18, 19 and 22-24 as being unpatentable over Freyer et al. in view of Reid (N. Engl. J. Med., 2002) and Iqbal (Expert Opin. Pharmacother.).

In the previous Response filed November 11, 2008, the Examiner argued that the results of Example 6 on page 50 of the specification were not commensurate in scope with the claims. Claims 18, 19 and 24 have been amended to better conform to the results described in Example 6 of the specification. Example 6, starting on page 50 of the specification describes the effectiveness of intravenous administration of zoledronic acid in preventing the bone loss and reduction of mechanical properties induced by aromatase inhibition or surgical ovariectomy in rats. The results showed a single iv injection of 0.8 µg/kg zoledronic acid delayed bone loss significantly for 24 weeks in patients treated with letrozole with the highest dose being full protective over the entire 24-week duration of the study, page 51 lines 6-10 of the specification. The findings of this study were summarized on page 52 of the specification:

> Discussion: Our data indicates for the first time that in rats, Zol dose-dependently protects against cancellous bone loss, corical thinning and reduction of bone strength induced by daily oral letrazole, at a dose of 20µg/kg, fully protects against letrozole induced bone loss for at least 24 weeks.

The newly amended claims are non-obvious over the cited references because it would not have been obvious to one of ordinary skill in the art at the time of the invention to have employed the administration of an aromatase inhibitor and a bisphosphonate as taught by

Freyer, using specifically zoledronic acid as the bisphosphonate and letrozole as the aromatase inhibitor. Applicants respectfully request the obviousness rejection be withdrawn from consideration. Entry of this Response is respectfully requested.

Respectfully submitted,

Oona Manzari

Novartis Pharmaceuticals Corp.
Patents Pharma
One Health Plaza, Building 101
East Hanover, NJ 07936-1080
(862) 778-7852

Oona A. Manzari
Attorney for Applicants
Reg. No. 48,152

Date: 3/9/09